European Medicines Agency

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QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE APPLICATION FOR A CHANGE TO THE MARKETING AUTHORISATION
for
TYGACIL

International non-proprietary name (INN): ***tigecycline***

On 22 April 2008, Wyeth Europa Limited officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a new indication for Tygacil, in the treatment of community-acquired pneumonia.

What is Tygacil?
Tygacil is a powder that is made up into a solution for infusion (drip into a vein). It contains the active substance tigecycline. Tygacil is an antibiotic that is already used to treat adults with complicated infections of the skin or soft tissue (the tissue below the skin) and complicated infections in the abdomen.

What was Tygacil expected to be used for?
Tygacil was also expected to be used to treat adults with community-acquired pneumonia. This is a serious type of lung infection that is caught outside of hospital. Community-acquired pneumonia is usually caused by infection with bacteria.

How is Tygacil expected to work?
The active substance in Tygacil, tigecycline, belongs to the group of antibiotics called 'glycylcyclines', which are similar to tetracycline. Tigecycline works by blocking the bacteria's ribosomes, the parts of the bacterial cells where new proteins are made. By blocking the production of new proteins, the bacteria cannot multiply and they eventually die. This is expected to help in the treatment of community-acquired pneumonia.

What documentation did the company present to support its application to the CHMP?
The effects of Tygacil were first tested in experimental models before being studied in humans.
The effectiveness of Tygacil was tested in two main studies involving a total of 846 adults who needed treatment in hospital for community-acquired pneumonia. Both studies compared Tygacil with levofloxacin (another antibiotic). Both antibiotics were given for up to two weeks. The main measure of effectiveness was the number of patients who were cured of their pneumonia within the three weeks after their last dose of antibiotic.
An additional study looked at the effectiveness of Tygacil in patients who had caught pneumonia in hospital.

How far into the evaluation was the application when it was withdrawn?
The application was at day 150 when the company withdrew. After the CHMP had assessed the responses from the company to a list of questions, there were still some unresolved issues outstanding.

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The CHMP normally takes up to 90 days to adopt an opinion after it has received an application for a change to a marketing authorisation. Following the CHMP's opinion, it usually takes around six weeks for the European Commission to update the licence.

What was the recommendation of the CHMP at that time?
Based on the review of the data and the company's response to the CHMP list of questions, at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Tygacil could not have been approved for the treatment of community-acquired pneumonia.

What were the major concerns that led the CHMP to recommend the refusal of the change to the marketing authorisation?
The CHMP was concerned that the patients included in the main studies may not have needed hospital treatment using medicines given intravenously (into a vein), so they did not match the types of patients for whom the medicine was intended. The Committee was also concerned over the number of deaths in patients receiving Tygacil with more serious infections, especially in the study of patients who had caught pneumonia in hospital. This raised doubts over whether Tygacil would be sufficiently effective in the treatment of patients with severe community-acquired pneumonia. The CHMP also had concerns over the measures that the company intended to put in place to minimise the risks associated with the medicine.
Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of Tygacil had not been sufficiently demonstrated and any benefits did not outweigh the identified risks.

What were the reasons given by the company to withdraw the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

What are the consequences of the refusal for patients in clinical trials using Tygacil?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials with Tygacil. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening for Tygacil for treatment of complicated skin and soft tissue infections and complicated infections in the abdomen?
There are no consequences on the use of Tygacil in the authorised indications, for which the balance of benefits and risks remains unchanged.